Tranylcypromine Withdrawal Phenomena

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The gradual or abrupt withdrawal of tranylcypromine can result in syndromes ranging in severity from mild discomfort to incapacitation. Five patients were subjected to the withdrawal of tranylcypromine. Vignettes describing the withdrawal syndrome experienced by these patients are presented. These patients suffered from severe depression or impairment of cognition in association with a reduction in their daily dose of tranylcypromine. The authors conclude that reductions in a patient's dose or the discontinuation of tranylcypromine warrant the careful supervision of a physician.

Key Words: antidepressants, depression, monoamine oxidase inhibitors, tranylcypromine, withdrawal

INTRODUCTION

Only two primary sources exist providing information about symptoms produced by the withdrawal of the monoamine oxidase inhibitor tranylcypromine (Le Gassicke et al 1965; Halle et al 1991). Le Gassicke et al (1965) described the course of a single patient who developed withdrawal symptoms after the substitution of a placebo for tranylcypromine. This patient abused the monoamine oxidase inhibitor; his dose varied between 200 mg and 750 mg daily. Halle et al (1991) recently noted that the withdrawal of tricyclic antidepressants and tranylcypromine can produce transient syndromes that are indistinguishable from major depression (American Psychiatric Association 1987). However, many other signs and symptoms developed among the five patients who were subjected to the withdrawal of this drug. The vignettes below highlight features of the syndromes produced by the withdrawal of tranylcypromine.

Case 1

Ms. A, a 40-year-old woman, presented with depressed and anxious mood, slowed mentation, agitation, insomnia, suicidal ideation, anhedonia and panic attacks. Her daily dose of tranylcypromine was increased to 40 mg over a two-day period. All symptoms remitted within a week. On the 18th day of treatment, she became euphoric, highly energized and hyperactive. Her daily dose of tranylcypromine was decreased to 20 mg. Twelve days later she became depressed and hypersomnic. She recovered rapidly, only to become depressed within three weeks.

It was concluded that Ms. A was rapid cycling, and tranylcypromine was discontinued. One day later she became confused and had difficulty organizing her thoughts and processing auditory information. She was also "jittery", "cold", and "anxious all day." These symptoms remitted within seven days.

Case 2

Ms. B, age 31, presented with depressed and anxious mood, poor concentration and memory, anergy, pathological guilt, hyperphagia and hypersomnia. She recovered when treated with 50 mg of tranylcypromine daily. Her daily dose was abruptly decreased to 30 mg. It was lowered to 10 mg one week later. She experienced depressed and anxious mood, initial insomnia, daytime somnolence, malaise, poor concentration, fatigue, anhedonia and nocturnal myoclonus for two to four days after each reduction in dose. These symptoms remitted within three weeks of the last dose of tranylcypromine.

Case 3

Mr. C, age 26, presented with a moderate to severe depressive syndrome. He had an excellent response to tranylcypromine before abruptly discontinuing treatment for seven

days. Two days later he became tearful, unmotivated, "slowed-down," fatigued, socially phobic and inattentive. He also suffered from headaches and was disturbed by intense, vivid dreams. He felt much better four days after resuming treatment with tranylcypromine.

Case 4

Ms. D is a 35-year-old woman who had a complete response when treated with 40 mg of tranylcypromine for major depression. Within two to three days of an abrupt decrease in her daily dose of tranylcypromine to 10 mg, she became depressed, tearful, unreactive and anhedonic, and suffered from slowing of her bodily movements and stream of thought, hand wringing, severe anxiety, tearfulness, hyperphagia and hypersomnia with concomitant middle insomnia. She had dreadful dreams that something tragic would befall her family. She stopped working. Although she had never before been suicidal, her husband was compelled to remain at home with her out of a deep concern that she would commit suicide.

Case 5

Mr. E, age 33, presented with depressed and anxious mood, poor concentration, fatigue, insomnia and anhedonia. His daily dose of tranylcypromine was gradually increased to 140 mg. After an unsuccessful four-month trial, the drug was discontinued over a ten-day period. He then became very anxious, fearful and weak.

Mr. E also developed previously unexperienced symptoms upon the withdrawal of tranylcypromine. He became hypersomnic and hyperphagic within two days of the last dose. He experienced difficulty carrying out tasks requiring complex organized motor skills, "scattered" unclear thought processes, and tingling sensations approximately six days after the last dose. He also suffered from nausea, sialorrhea, tremor, myoclonus, derealization and psychomotor retardation and agitation, "jitteriness", extreme fear when interacting with others and flushing.

DISCUSSION

Each of the patients developed symptoms of a depressive syndrome within days of a decrease in their dose of tranylcypromine; the severity of the syndrome exceeded that which prompted treatment. The patients also developed moderate to severe cognitive impairment. These two features are not characteristic effects of the withdrawal of heterocyclic antidepressants (Dilsaver et al 1983a; 1983b; Dilsaver et al 1987; Dilsaver and Greden 1984a). This difference is not unexpected. The pathophysiological events underlying the genesis of heterocyclic antidepressants (Dilsaver 1990; Dilsaver and Greden 1983; Dilsaver and Greden 1984a; 1984b; Dilsaver et al 1983; 1987) and tranylcypromine (Dilsaver 1988) withdrawal phenomena are categorically distinct. Dilsaver (1988; 1990) has observed that the discontinuation of tranylcypromine produces syndromes similar to those caused by the withdrawal of amphetamine. Tranylcypromine is converted in the body to amphetamine. This may result in changes within the limbic system similar to those underlying amphetamine dependence. A detailed account of the pathophysiology of the withdrawal syndromes is given in the above-cited articles.

It is recommended that reductions in a patient's daily dose of tranylcypromine be carefully supervised. It seems prudent to discontinue this drug over a period of weeks to months, if possible.

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